REMARKS

This Amendment is in response to the Office Action, dated October 28, 2009 ("Office Action"). It is respectfully submitted that the application is in condition for allowance. Claims 1-42 are pending; claim 23 having been amended and claims 1-22 and 24-37 having been previously withdrawn. No new matter has been added. Allowance and reconsideration of the application in view of Applicants' amendment and the ensuing remarks are respectfully requested.

Claim 23 has been amended to indicate that IVD is abbreviated for intervertebral disc. No new matter is added.

Claims 23 and 38-42 are rejected under 35 U.S.C. §103(a) as allegedly being unpatentable over Sanchez-Ramos *et al.* (*Experimental Neurology*, 164:247-256, 2000) in view of Hutton *et al.* (*Clinical Biomechanics*, 16:728-734, 2001, "Hutton 1"), Hutton *et al.* (*Spine*, 24(15):1507-1515, 1999, "Hutton 2"), and Richardson *et al.* (*European Cells and Materials*, 6:Suppl. 2, 20, 2003) for reasons of record.

Particularly, the Examiner asserts that Sanchez-Ramos *et al.* teaches human bone marrow stromal mesenchymal stem cells induced to differentiate into neural cells under experimental culture conditions. The Examiner also asserts that Hutton 1 teaches exposure to specific values of hydrostatic and atmospheric pressures to directly affect the synthesis of collagen and proteoglycan in IVD cells. The Examiner further states that "the more useful comparison it [sic] would be to compare 1MPa with 0.35 MPa…under reduced oxygen tension of 6%." The Examiner asserts that Hutton 2 teaches that further studies are needed to examine whether other values of hydrostatic pressure applied would affect cell synthesis of collagen and proteoglycan markers. The Examiner additionally asserts that Richardson *et al.* teaches culture of human mesenchymal stem cells in alginate gel and induced to differentiate along a chondrocytic phenotype for use as a source of chondrocytes for repair of degenerate IVD. Applicants respectfully traverse this rejection.

An applicant's disclosure of his or her own work within the year before the application filing date cannot be used against him or her as §102(a) prior art. MPEP

§2132.01 (citing *In re* Katz, 687 F.2d 450, 215 USPQ 14 (CCPA 1982)). As such, in instances wherein the applicant is one of the co-authors of a publication cited against his or her application, the publication may be removed as a reference by submission of a specific declaration by the applicant establishing that the article is describing an applicant's own work. Id.

Applicants submit that the priority date of the pending claims is March 2, 2004, the filing date of Application No. GB 0404656.1. (See e.g., claims 1, 5, and 9 of GB 0404656.1) Pursuant to PCT Rule 17, a certified copy of Application No. GB 0404656.1 was received by the International Bureau on April 26, 2005. Applicants submit that Richardson *et al.*, published September 2003, is not prior art under §102(a) or §102(b). Submitted herewith is a declaration by one of the applicants, Stephen M. Richardson, which shows that to the extent that the instant invention is described in Richardson *et al.*, it describes solely the work of Stephen Richardson, Christine Le-Maitre, Anthony John Freemont, and Judith A. Hoyland. The additional named authors in Richardson *et al.* are co-authors of the article, but did not make any inventive contribution to the subject matter of Richardson *et al.* and are not co-inventors of the instant application. Accordingly, Richardson *et al.* is not prior art under §102(a) or §102(b). Since Richardson *et al.* cannot be used as §102(a) or §102(b) prior art, it cannot be used as a prior art reference to form a §103(a) rejection. The Examiner's §103(a) rejection relies on Richardson *et al.* in combination with Sanchez-Ramos *et al.*, Hutton 1 and Hutton 2. Thus, without Richardson *et al.*, the Examiner has not made a *prima facie* showing of obviousness and the rejection fails. Applicants respectfully request reconsideration and withdrawal of the rejection under §103(a).

Notwithstanding the above, Applicants wish to note that Applicants do not agree with the Examiner's findings, interpretation and conclusions drawn from Richardson *et al.* Additionally, in the interest of advancing prosecution and in no way conceding to the merits of the Examiner's rejections, Applicants offer the following remarks regarding Sanchez-Ramos *et al.*, Hutton 1 and Hutton 2.

To establish a *prima facie* case of obviousness, the Examiner must clearly articulate the reason(s) why the claimed invention would have been obvious. KSR International Co. v. Telefex Inc., 550 U.S. 398, 82 USPQ2d 1385 (2007); MPEP §2142.

Furthermore, "the mere fact that references can be combined or modified does not render the resultant combination obvious unless the results would have been predictable to one of ordinary skill in the art." MPEP §2143.01 (citing KSR International Co. v. Telefex Inc., 550 U.S. 398, 82 USPQ2d 1385 (2007)). As such, a "reasonable expectation of success is required." MPEP §2143.02.

Reconstruction based on hindsight reasoning may be proper if takes into account only knowledge which was within the level of ordinary skill in the art at the time the claimed invention was made and does not include knowledge gleaned from an applicant's disclosure. *See* In re McLaughlin, 443 F.2d 1392, 1395 (CCPA 1971). Furthermore, the Examiner must not lose sight of whether it would have been obvious to combine the references without having access to the application to arrive at the claimed invention. It is impermissible hindsight to use the present application as a template to piece together prior art teachings to allege obviousness. *See In re* Fritch, 972 F.2d 1260, 1266 (Fed. Cir. 1992).

Applicants submit that one of skill in the art would not combine Sanchez-Ramos *et al.*, Hutton 1 and Hutton 2 and even if these references are combined, which Applicants in no way concede that it is appropriate, the combination does not render the claimed invention obvious.

First, the Examiner has not clearly articulated any reason as to why the claimed invention would have been obvious in light of Sanchez-Ramos *et al.*, Hutton 1 and Hutton 2. The Examiner merely summarizes Sanchez-Ramos *et al.*, Hutton 1 and Hutton 2 and allege that one of skill in the art would have been motivated combine these references to reach the claimed invention.

Second, Applicants submit that the Examiner has mistakenly interpreted the relevance of the prior art references' teaching on the patentability of the claims; that is, The Examiner has not shown how Sanchez-Ramos *et al.*, Hutton 1 and Hutton 2 are relevant to the method of differentiating human mesenchymal stromal stem cells toward IVD cells.

Sanchez-Ramos *et al.* was cited as teaching a method of differentiating human bone marrow stromal mesenchymal stem cells into neural cells. The Examiner alleged

that Sanchez-Ramos *et al.* "differs from the present invention for not teaching the MSSCs encapsulated in a gel to increasing pressures up to 30 psi and reduced oxygen pressure." However, the presently claimed invention relates to differentiating human stromal mesenchymal stem cells into IVD cells, **not** neural cells. Unmistakably, there is no teaching or suggestion by Sanchez-Ramos *et al.* on how bone marrow stromal mesenchymal stem cells can be or should be differentiated into IVD cells. Accordingly, one of skill in the art would not look to Sanchez-Ramos *et al.* for its teachings to combine with Hutton 1 and Hutton 2 to arrive at differentiating human mesenchymal stromal stem cells into IVD cells. Hutton 1 and Hutton 2 also do not provide the requisite teaching or suggestion and the Examiner has not appropriately identified any teaching or suggestion in the prior art. Further, the difference between Sanchez-Ramos *et al.* and the present invention identified by the Examiner is not the only difference. At best, the relevance of Sanchez-Ramos *et al.* on the present invention is merely its disclosure regarding the existence of human bone marrow stromal mesenchymal stem cells.

The Examiner's allegations regarding the relevance of Hutton 1 and Hutton 2 are also mistaken. The disclosures by Hutton 1 and Hutton 2 relate to mature IVD cells. The implication of how mature IVD cells react to being exposed to increased pressures has no bearing on how mesenchymal stromal stem cells would react to increased pressures, or on producing IVD cells from a different type of cell. Particularly, it has no bearing on methods for the differentiation of mesenchymal stromal stem cells towards IVD cells. One of skill in the art would not extrapolate the findings regarding mature IVD cells described by Hutton 1 and Hutton 2 to methods for the differentiation of mesenchymal stromal stem cells because there is no relevance between how mature IVD cells responded and the promotion of mesenchymal stromal stem cells differentiating toward IVD cells. Additionally, Hutton 1 and Hutton 2 make no teaching or suggestion of regarding the exposure of other types of cells to increased pressures, or the exposure of increased pressures on other types of cells to promote differentiation of stem cells toward IVD cells. One of skill in the art would not look to Hutton 1 or Hutton 2 to combine with other prior art teachings to arrive at a method of differentiating mesenchymal stromal stem cells towards IVD cells.

Furthermore, Hutton 1's disclosure of 6% oxygen in 0.35 MPa also bears no relevance to the differentiation of mesenchymal stromal stem cells towards IVD cells. The disclosure was made in the context volumetric analysis when the partial pressure of O_2 and CO_2 are kept the same as in atmospheric conditions. Furthermore, the subject matter of the study is mature IVD cells. There were no observations or conclusions attributed to the 6% oxygen environment. One of skill in the art would not extrapolate the disclosure that the mature IVD cells were exposed a 6% oxygen environment to having beneficial effects on mesenchymal stromal stem cells because there is no indication that it would promote differentiation toward IVD cells. The examiner has not identified any teaching or suggestion that would lead one of skill in the art to apply the methods performed on mature IVD cells to mesenchymal stromal stem cells in order to promote differentiation towards an IVD cell.

Third, the combination of the prior art teachings is simply flawed as one of skill in the art would have no reason to combine these teachings. Even if one of skill in the art would combine these teachings, which Applicants in no way concede to, the combination of the prior art does not lead to any predictability regarding the effects on mesenchymal stromal stem cells; namely, that they can be differentiated toward IVD cells. The Examiner has not identified any teaching or suggestion of using mesenchymal stromal stem cells as the starting material to differentiate towards IVD cells. The Examiner has not identified any teaching or suggestion that mesenchymal stromal stem cells will differentiate towards IVD cells when exposed to increasing pressures. The Examiner has not identified any teaching or suggestion that mesenchymal stromal stem cells will differentiate towards IVD cells when exposed to reduced oxygen tension. Thus, there is no predictability regarding how mesenchymal stromal stem cells will respond to these conditions.

Fourth, one of skill in the art would have no expectation that mesenchymal stromal stem cells can be successfully differentiated toward IVD cells. The Examiner quotes the prior art in detail; however, the identified disclosures have no relevance to the instant technology. Even combining Sanchez-Ramos *et al.*, Hutton 1 and Hutton 2 as the Examiner has alleged, which Applicants do not concede as being proper, there simply would not be any expectation of success.

Fifth, Applicants respectfully submit that the Examiner has taken Applicants' application and pieced together the prior art in a nonsensical manner to arrive at Applicants' claimed invention. Such reconstruction is impermissible hindsight reconstruction. For example, without the knowledge that mesenchymal stromal stem cells can be used to differentiate towards IVD cells, there would not be any reason to look to Sanchez-Ramos *et al.*; although, Applicants maintain that Sanchez-Ramos *et al.* is irrelevant. Without the knowledge that increasing pressures or reduced oxygen tension would promote differentiation of mesenchymal stromal stem cells towards IVD cells, there would not be any reason to look to Hutton 1 or Hutton 2. Similarly, Applicants maintain that Hutton 1 and Hutton 2 are irrelevant because, among other things, they pertain to mature IVD cells.

In light of the foregoing, all of the claims in the application are now believed to be allowable. Favorable consideration and a Notice of Allowance are earnestly solicited. If for any reason Examiner finds the application other than in condition for allowance, Examiner is requested to contact the undersigned attorney at the Los Angeles telephone number (213) 633-6800 to discuss the steps necessary for placing the application in condition for allowance.

Respectfully submitted,
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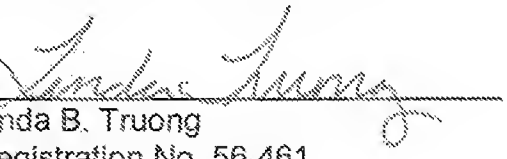
By: 
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